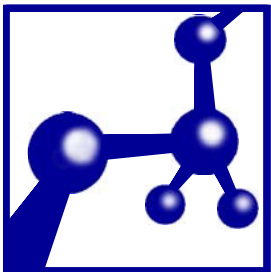




ASTM Medical Device Cleaning:

Design, Clean, Verify

Stephen Spiegelberg



**Cambridge
Polymer Group, INC.**

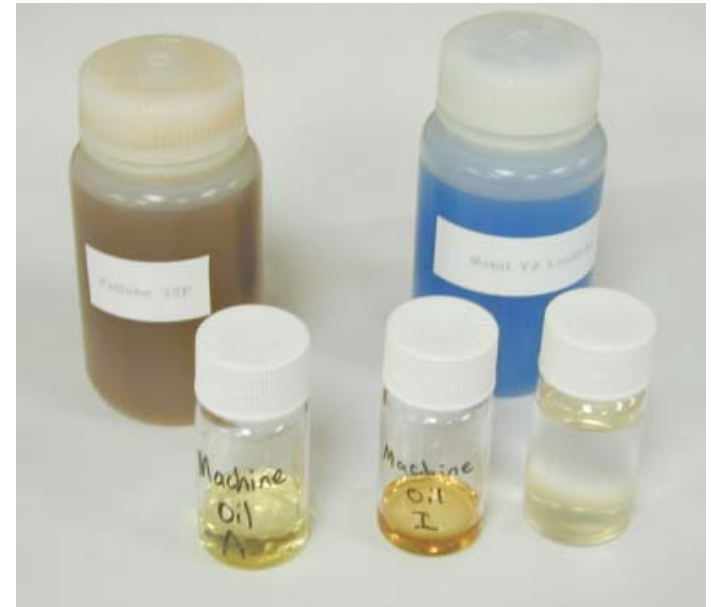
Consultation, Testing, and Instrumentation for Polymeric Materials

History: ASTM Activities

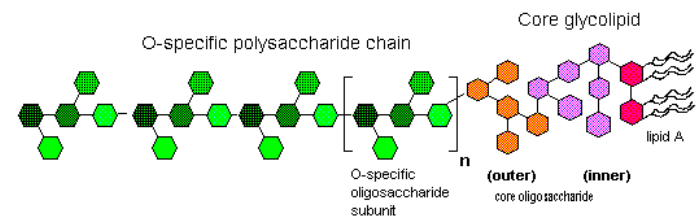


American Society for Testing and Materials

- Sulzer Interop Recall in 2000



~2000 revisions due to lack of osseointegration
\$1B class action settlement

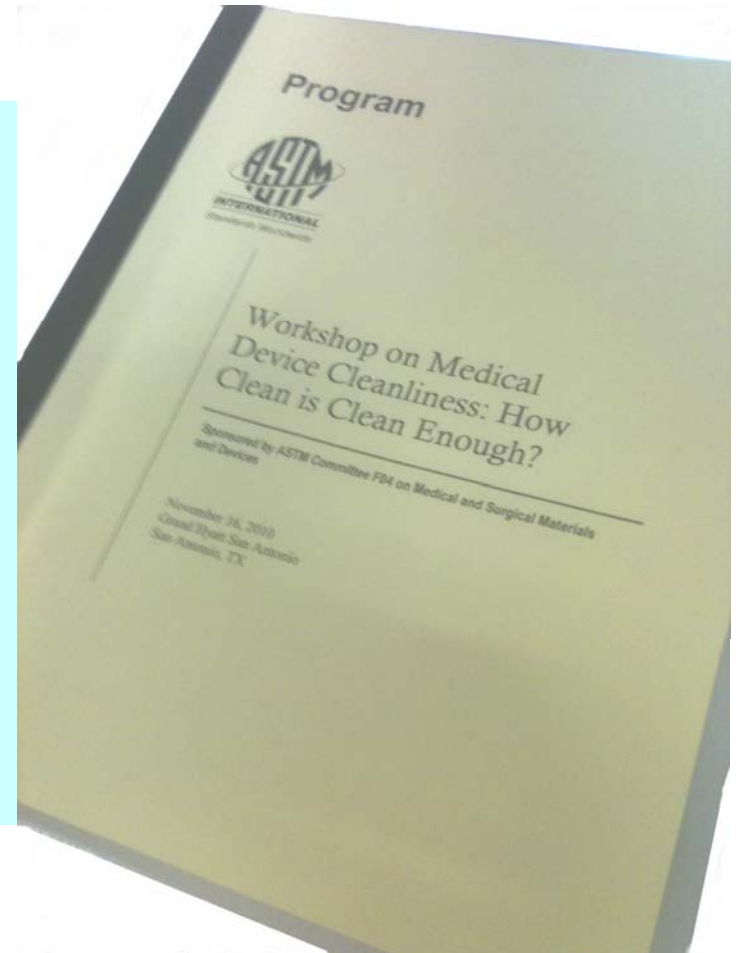




ASTM Activities on Cleanliness



- Workshop on Device Cleanliness (May, 2003)
 - Start of F04.15.17 (Device Cleanliness)
- Symposium on Device Cleanliness (May, 2005)
- Workshop on “How Clean is Clean Enough?” (November 2010)
 - Start of 4 new cleaning standards





ASTM Activities on Cleanliness

- **Verify**
 - How to quantify residues on implants
- **Clean**
 - How to validate clean lines and provide guidance
- **Design**
 - How to design implants with cleaning in mind



Design - Considerations

- Single use or re-usable?
- What materials are used in device?
- What manufacturing materials will be used that could leave residues?
- What cleaning systems are available for use?

Cleaning should be part of the design input process

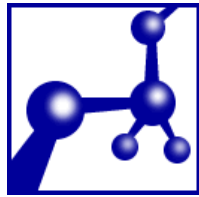
Design – Single Use or Re-usable?



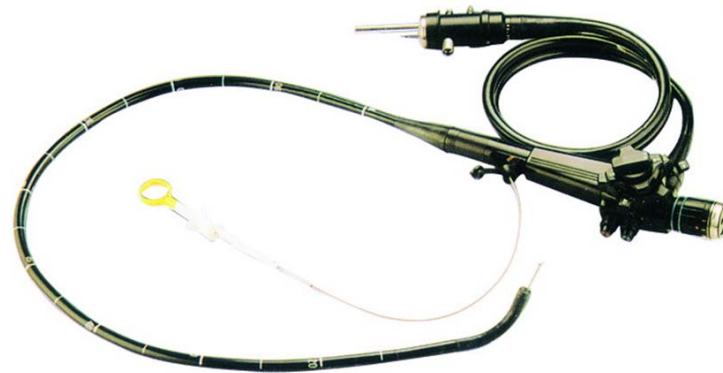
- Cleaned by manufacturer
- Components only exposed to a single cleaning cycle
- Known manufacturing residues to be removed during cleaning
 - Polishing compounds, lubricants, coolants, buffers



Design – Single Use or Re-usable?



- Cleaned by reprocessor or hospital
- Exposure of components to tissue and fluids
- Cleaning and disinfection require access to surfaces
 - Design for disassembly and cleaning
- Adequate instructions for reprocessing
 - Potential damage to component during cleaning
 - How many times can it be reprocessed?

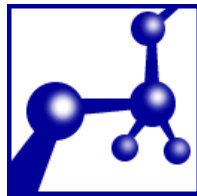




Design to Minimize Cleaning

- **Design components for simple, effective cleaning**
 - Blind spots
 - Mixed materials (what cleaning agents can be used on them)
 - Sharp corners, fine features, threading
 - Disassembly of re-usable parts for cleaning
- **Design components for simple manufacturing**
 - Fewest manufacturing steps
 - Fewest number of processing compounds (grit blast, polish, masking)
- **Design simplest cleaning operation**
 - Omnidirectional cleaning vs. directional
 - Avoiding redepositing removed soil on clean parts
 - Cleaning your clean-line
 - Cross-contamination of different components cleaned in the same clean-line
- **Design with cleaning validation in mind**
 - How to assess how clean your parts are?

Design: ASTM Activities



Work Item Number: WK31799

Date: May 9, 2011

Standard Practice/Guide for Designing Medical Devices for Cleanability

This standard is issued under the fixed designation XXXXX; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ϵ) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This guide is intended to provide design criteria for manufacturers of reusable medical devices that will minimize debris retention and ease the removal of contaminants from devices.

1.2 *Include in this section the system of units to be used. Refer to the above ASTM Standards Units toolbar button for a dropdown menu of ASTM's Form and Style Manual statements.*

1.3 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and*



Design: ASTM Work Item 31799

- Serrated edges
- Hinges
- Acute angles
- Coils
- Junctions between insulating sheaths
- Long or narrow opaque lumens
- Blind ends
- Threaded areas



Cleaning systems

Cleaning



- Adequate removal of soils without introducing new residues
 - Cleaning agents
 - Migration of residues from one location to another
 - Elution/extraction
- Damage to component or materials
 - Mechanical, thermal, chemical
- Validation of cleaning process
- Cost and process time
- Cross-contamination
 - Multiple product lines





Cleaning: Considerations

cleaning materials

- Water
- Detergents
- Surfactants
- Buffers
- Chelators
- Enzymes

cleaning systems

- Ultrasonics
- Water jets
- Refluxing
- Baths
- Mechanical (brush)

effectiveness in removing residues

vs.

damage to components



Cleaning: Single Use

- Validating cleaning lines
- FDA: Validation of Cleaning Processes (7/93) – pharmaceutical primarily
 - Equipment design
 - Written procedures
 - Analytical verification
 - Sampling
 - Establishment of limits

New ASTM work item

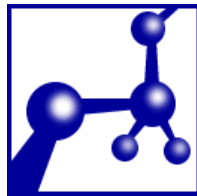


Cleaning: Clean-line Validation

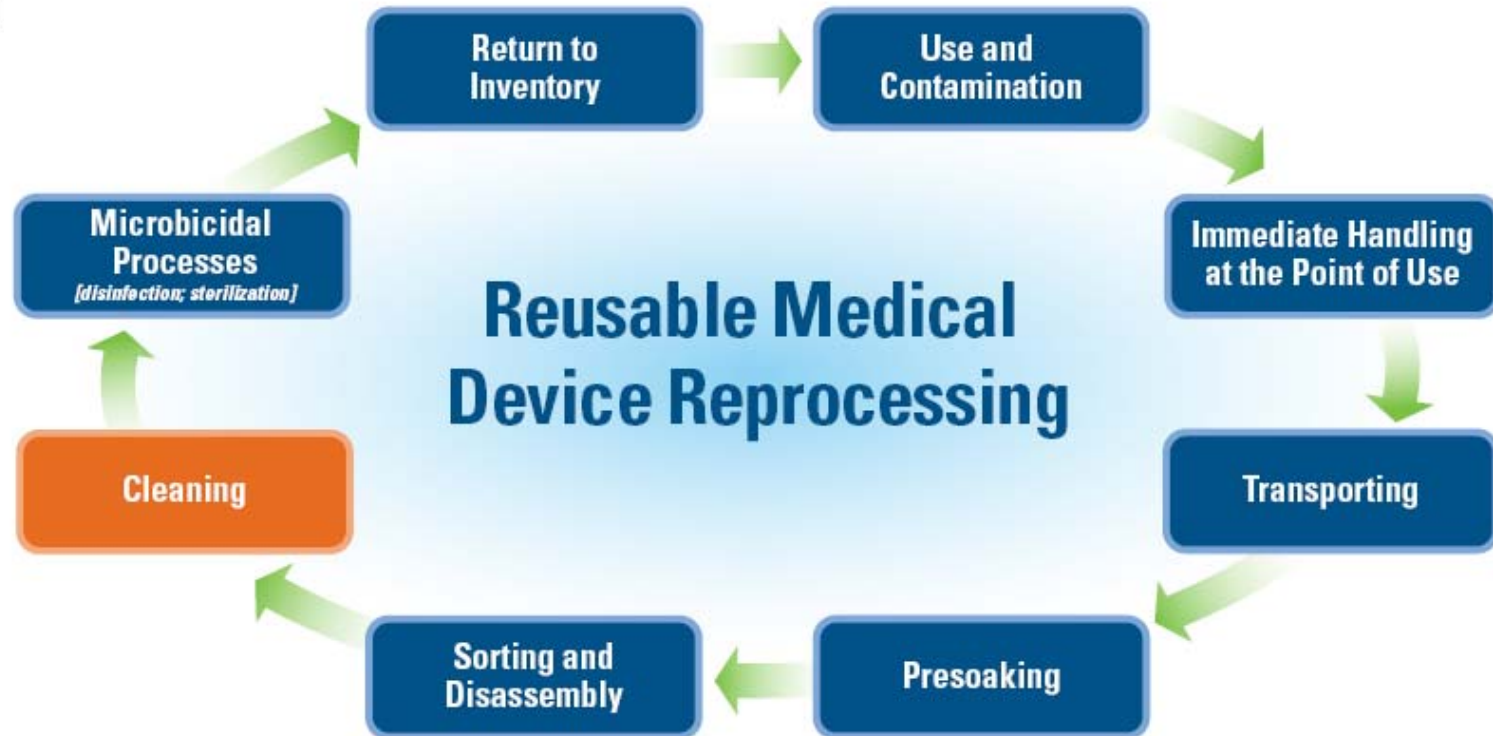


- Worst case analysis
 - Residues (test soils)
 - Devices
- Sample configuration
 - Device vs. coupon
- Choosing analytical method to verify cleanliness
 - Test frequency
 - Validation of method
 - Sample size (statistics)
- Monitoring cleaning system in real-time/batch
- When/how should a clean-line be re-validated
- Acceptance criteria

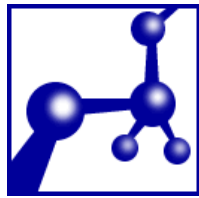




Cleaning: Re-usable Devices

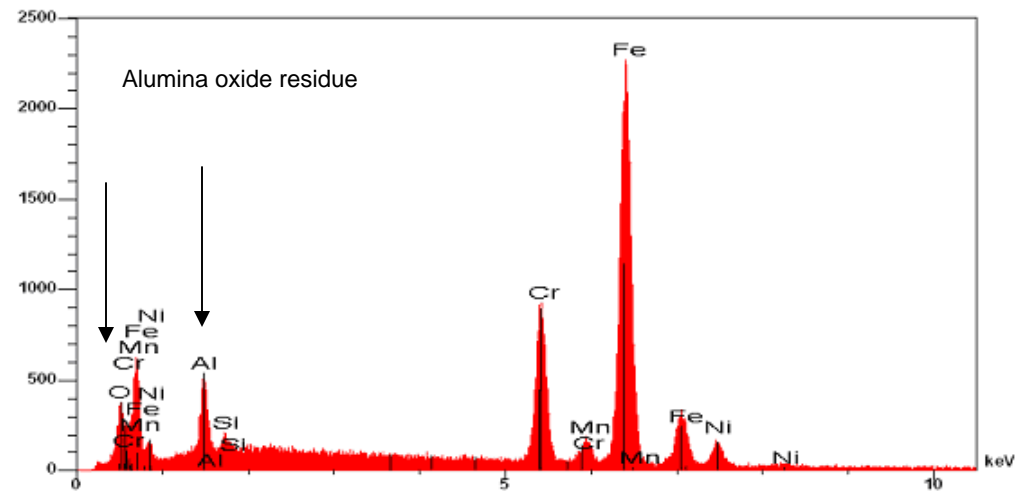
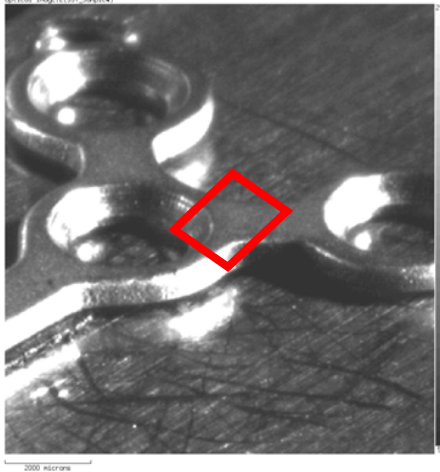


Adequate instructions for disassembly and cleaning

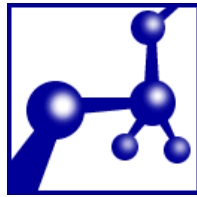


Verify: Is cleaning successful?

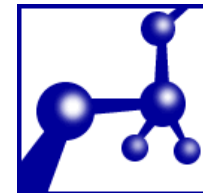
- Test methods
- Establishing acceptable limits



Verify: *ASTM Activities*



- **ASTM F2459** - Standard Test Method for Extracting Residue from Metallic Medical Components and Quantifying via Gravimetric Analysis
- **ASTM F2847** - Standard Practice for Reporting and Assessment of Residues on Single Use Implants
- **ASTM E2314** - Standard Test Method for Determination of Effectiveness of Cleaning Processes for Reusable Medical Instruments Using a Microbiologic Method (Simulated Use Test)
- **ASTM D7225** - Standard Guide for Blood Cleaning Efficiency of Detergents and Washer-Disinfectors



Verify: ASTM F2459

Standard Test Method for Extracting Residue from Metallic Medical Components and Quantifying via Gravimetric Analysis

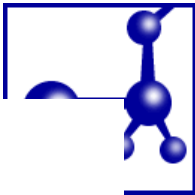
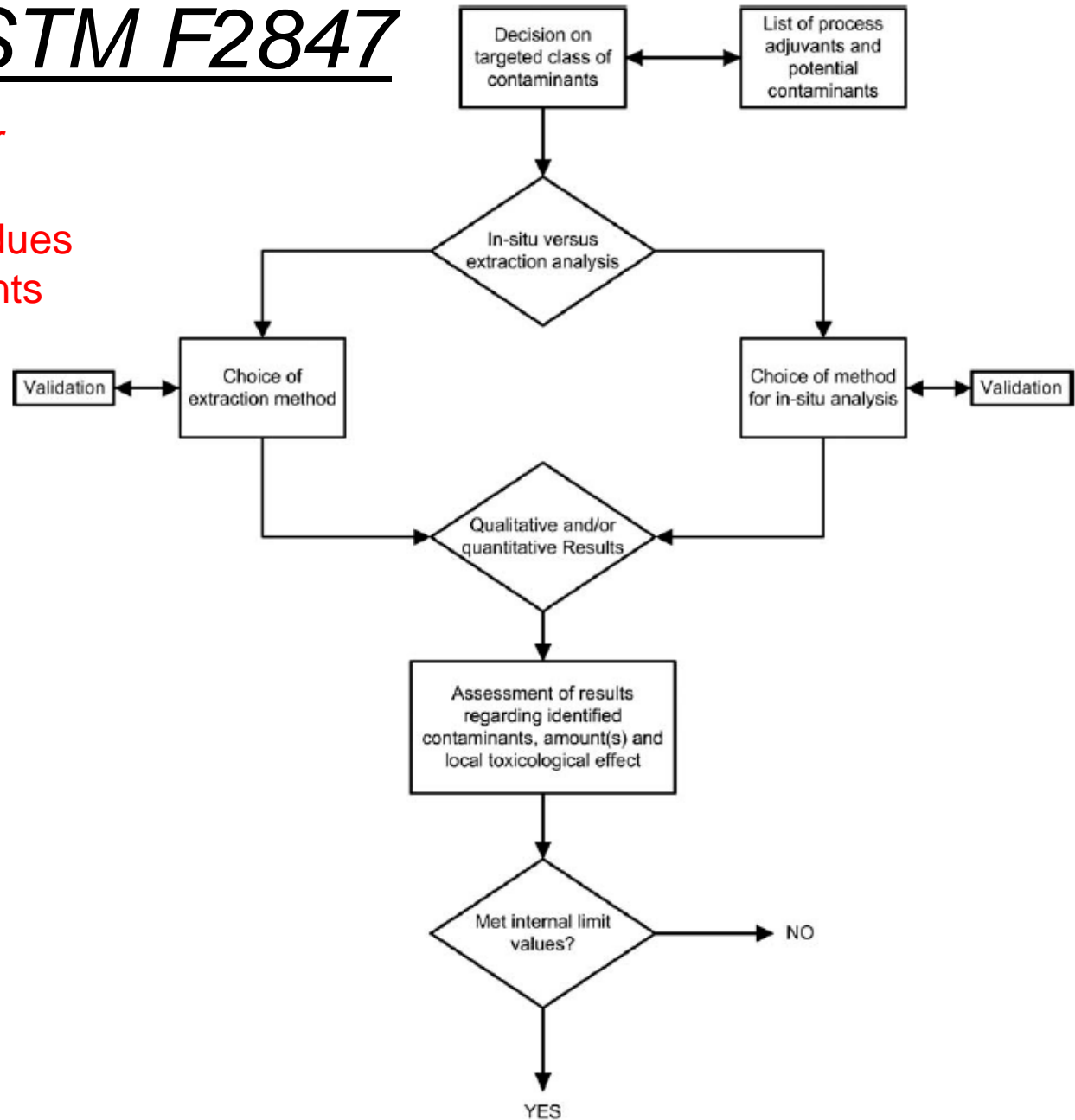
- Describes extraction protocol
 - Ultrasonic bath
 - Reflux
 - Extraction efficiency
- Gravimetric assessment of soluble and insoluble residue

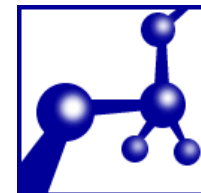


Verify: ASTM F2847

Standard Practice for
Reporting and
Assessment of Residues
on Single Use Implants

*Decision tree for
sample preparation
and analysis*





Verify: ASTM F2847

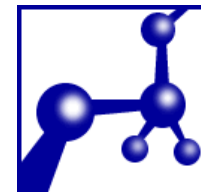
TABLE X1.1 Analytic Methods and Use—Non-exhaustive

NOTE 1—Methods in bold are described briefly in subsequent paragraphs.

NOTE 2—Some of the listed methods allow only for quantification of residues. The identification of residues requires often the combination of several analytical methods.

NOTE 3—Some more detailed information on different approaches and test methods is found in literature (1, 3-10).

Method(s)	Recommended for:				Suggested Standards
	Organics	Inorganics	Particulates	Biologics	
GC-MS/GC-TOF	X				PhEur 2.2.28/2.2.44
TOC	X				PhEur 2.2.44
RAMAN	X	X		X	PhEur 2.2.48
FTIR	X	X		X	PhEur 2.2.24
UV/Vis	X	X		X	PhEur 2.2.25
ICP-OES/ICP-MS		X			EPA 200.7 PhEur 2.2.57 PhEur 2.2.58
HPLC	X			X	PhEur 2.2.29
AAS		X			PhEur 2.2.23
EDS / EDXA		X	X		
Bioburden				X	ISO 11737-1
Endotoxin				X	USP<85> AAMI ST72
SEM			X		
Auger (AES)		X	X		ASTM E996
XPS (ESCA)	X	X	X		ASTM E996
TOF-SIMS	X	X	X		ASTM E1504
Optical Inspection	X	X	X		
Gravimetric	X	X	X		ASTM F2459
Peptides				X	PhEur 2.2.55



Verify: ASTM F2847

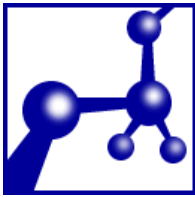
TABLE 1 Suggested Table for Reporting of Residues

NOTE 1—The reported table shall reflect the mean value of all measurements of a product and the error including the error of the method.

NOTE 2—The column Applied Analytical Method exemplifies methods and applicable standards. They can be replaced by any method/standard protocol suitable for the particular residues.

Categories	Results of Analysis	Set Limit Values	Detection Limit	Applied Analytical Methods
Inorganic	[mass/implant] [mass/surface area]	[mass/implant] [mass/surface area]	[mass/implant] [mass/surface area]	ICP-OES (PhEur 2.2.57)
Organic				GC-MS (PhEur 2.2.28 , EPA 8270C)
Biological				e-spray MS (PhEur 2.2.43)
Bioburden	[CFU/implant]	[CFU/implant]	[CFU/implant]	ISO 11737-1
Endotoxin	[EU/implant]	EU/implant ^A	[EU/implant]	USP<85> AAMI ST72
Particulate	[mass/implant] [mass/surface area] [Number/implant] or [cm ² /cm ²] [Atomic-%] or [Molecular-%]	[mass/implant] [mass/surface area] [Number/ implant] or [cm ² /cm ²] [Atomic-%] or [Molecular-%]	[mass/implant] [mass/surface area] [Number/implant] or [cm ² /cm ²] [Atomic-%] or [Molecular-%]	SEM (internal protocol) XPS (ASTM E996)
Visual Inspection	[Optical observations]	[Optical observations]	[Optical observations]	(internal protocol)

^A Limit value as defined for device types listed in **FDA** Guidance for Industry and Guideline on Validation of the Limulus Amebocyte Lysate Test as an End-Product Endotoxin Text for Human and Animal Parenteral Drugs, Biological Products, and Medical Devices (December 1987).



Verify: Test Soils

- New ASTM work item
- Standardized test soils
- Validate
 - Clean lines
 - Test methods (and establish detection limits)



Verify: Test Soils

Work Item Number: 33439

Date: 5/25/2011



Standard Practice/Guide for Standard test soils for validation of cleaning methods for reusable medical devices^a

This standard is issued under the fixed designation XXXXX; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ϵ) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This document describes standard test soils that can be used to test the efficacy of cleaning systems for re-processing of re-usable medical devices. The provided test soil recipes are not intended to encompass every biological residue with which a medical device is likely to come into contact.

1.2 Include in this section the system of units to be used. Refer to the above ASTM Standards Units toolbar button for a dropdown menu of ASTM's Form and Style Manual statements.

1.3 This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.



Verify: ASTM WK 33439

- Test Soils

- Blood analog
- GI fluid analog

Formulas and shelf life

- Use for cleaning testing

- Apply the soil on a test device by a pipette tip, painting the soil onto the device using a brush, or by immersing the device in the test soil.
- Dry for up to 24 hours
- Fix with glutaraldehyde

Increasing cleaning challenge

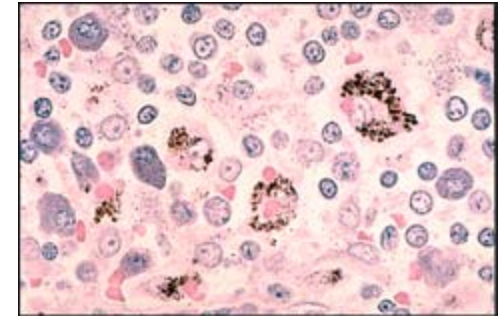
How Clean is Clean Enough?





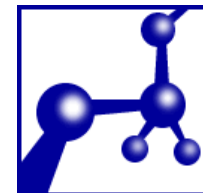
Verify: Establishing Residue Limits

- WK32535: Establishing Limit Values for Residues on Single use Implants
 - Biocompatibility
 - Baseline measurement of currently marketed implants
 - Field reports of success/issues
 - Clinical success = acceptable limits
 - Biocompatibility
 - Animal studies, cytotoxicity studies
 - Achievable with clean-line
 - Statistics
 - Cost



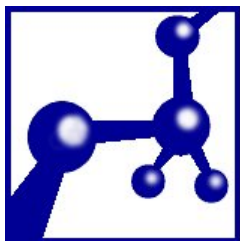
FDA does **not intend to set acceptance specifications** or methods for determining whether a cleaning process is validated. The firm's rationale for the **residue limits** established should be logical based on the manufacturer's knowledge of the materials involved and be **practical, achievable, and verifiable**. (Validation of Cleaning Processes (7/93))

For More Information



ASTM Task Group F04.15.17

November 16th, 2011 (Tampa, FL)



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